SKIN CANCERS AMONG ADULT PATIENTS ATTENDING THE OCEAN ROAD CANCER INSTITUTE IN DAR ES SALAAM – PREVALENCE, PATTERN, CLINICAL PRESENTATION AND FACTORS ASSOCIATED WITH TREATMENT OUTCOMES

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A dissertation Submitted in (partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences

October, 2024

CERTIFICATION

The undersigned certifies that, he has read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation titled “Skin cancer among adult patients attending the ocean road cancer institute in Dar Es Salaam –pattern, clinical presentation, treatment outcomes and their associated factors” in fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences

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ABSTRACT

Background: Skin malignancies are a cause of significant morbidity and mortality globally, although they are generally under-reported in most parts of Africa. In Tanzania, a study conducted in 2018 reported commonest cancers to be Malignant Melanoma (65%), Kaposi's sarcoma (10.4%), Squamous cell carcinoma (8.4%) and basal cell carcinoma (7.8%). Other non-melanoma skin cancers are not well documented. With the ongoing efforts to prevent and improve care for patients with skin cancers in the country, not much is known about the current pattern, clinical presentation, outcomes of treatment, and the factors associated with such outcomes.

Objectives: To describe the prevalence, pattern, clinical presentation, treatment modalities offered, outcomes of treatment offered and factors associated with outcomes of treatment among patients presenting with skin malignancies at the ORCI.

Methodology: This was a hospital based retrospective cohort study which was carried out at the Ocean Road Cancer Institute (ORCI) in Dar es Salaam, Tanzania. Adult patients who were 18 years and above with a confirmed diagnosis of skin cancer attended from January 2019 to October 2023 were systematically selected from the hospital database and medical records to the desired sample size of 480. A structured Questionnaire was used for data entry. Descriptive statistics were used to summarize the data, while factors associated with outcome of treatment were analyzed initially using a univariate analysis, and then a multivariate analysis for variables with p-values < 0.2. Kaplan Meir curves were used to describe survival. A p-value less than 0.05 was regarded as statistically significant.

Results: A total of 480 patients were enrolled. Kaposi's Sarcoma was the most prevalent cancer accounting for 57% of cases (95% CI: 53% - 62%). This was followed by Squamous Cell Carcinoma at 22% (95% CI: 18% - 26%). Kaposi's Sarcoma predominantly manifested on the lower limbs (79.6%). Clinical presentation of the different skin cancer types varied according to the type of cancer. Kaposi's Sarcoma

presented with irregular multiple nodular lesions in (36%) of patients, lesions were commonly hyperpigmented (47.3%), and most had an irregular, nodulated surface (21.5%). Malignant Melanoma was characterized mostly by irregular and roundish lesions (39 % and 31.7% respectively), and most lesions were hyperpigmented (48.8%).

The median duration between first symptom onset and definitive treatment initiation was 6 months. Prevalence of HIV among the patients was high (22.9%). The overall mortality was 11.3%, being higher (14.5%) among HIV positive patients. The overall one–year survival rate of patients with skin cancer at the ORCI was 90.7%. Patients with no education had significantly lower odds of being cured compared to those with other education levels (Odds Ratio of 0.1 [(95% CI = 0.01 - 0.88,0 p = 0.038]).

Conclusion: During the study period, the most common skin cancer was Kaposi's Sarcoma. There was high mortality among those who were HIV positive. Most patients received treatment rather late, but had good survival and patients treated by radiotherapy had better outcome. There is need for emphasis on formal educational for better treatment outcomes.

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ABBREVIATIONS

AK	Actinic keratosis
BCC	Basal cell carcinoma
BMC	Bugando Medical Centre
CIS	Carcinoma In Situ
CM	Skin cancers
FBP	Full Blood Picture
HDI	Human Development Index
HIV	Human immunodeficiency Virus
KS	Kaposi's sarcoma
MMSC	Malignant Melanoma Skin Cancer
MNH	Muhimbili National Hospital
NHIF	National Health Insurance Fund
NMSC	Non-Melanoma Skin Cancers
ORCI	Ocean Road Cancer Institute
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
UVR	Ultra violet radiation
WHO	World Health Organization

DEFINITION OF TERMS

Skin cancer	According to WHO Skin cancer is defined as an out-of-control growth of abnormal cells in the epidermis, the outermost skin layer, caused by unrepaired DNA damage that triggers mutations. The term is used interchangeably with skin/cutaneous cancer.
Pattern of skin cancer	Refers to the frequency of skin cancers and presentation of the in different body parts among patients who presented in the hospital for treatment.
Chronic Skin Ulcer	Are areas of deprived skin tissue exposing the sub dermis and dermis.
Survival rate	Is the proportion of people in a study or treatment group still alive at a given period of time after diagnosis and or completion of treatment.
Relative Survival Rate	Is a technical way of comparing the survival of people who have a specific disease with those who don' have it, over a certain period of given time.
Survival time	Is the proportion of people in a study or treatment group still alive at a given period of time after diagnosis.
Treatment outcome	Is a change in the health status of an individual or a group of patients, which can be attributed to medical, surgical or radiological intervention. Some of the measurable treatment outcomes for skin cancer are remission of symptoms, complete eradication of the tumor and tumor free margin after surgery alone or surgery combined with radiotherapy.
Remission of symptoms:	Refers to the decrease in size of the tumor, decrease in pain or bleeding and tumor free margin after surgical

	excision
Types of skin cancer;	Types of skin cancer considered according to histopathological diagnosis.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Skin cancers are responsible for a significant morbidity and mortality, as well as causing significant economic burden globally. In 2018 the burden of skin cancers was reported as being 197.9 per 100,000 in both genders with more prevalence in males than in females (1). In Africa a systematic review done and reported on cancer statistics from different parts of Africa has reported that the commonest skin cancer in Sub-Saharan African countries with darker skin colour is Squamous cell carcinoma (SCC), while Basal cell carcinoma (BCC) was commoner in patients from North African countries who have a lighter skin colour. According to data from a study conducted in the year 2018, Malignant melanoma was the commonest (67.5%) skin cancer in Tanzania, followed by Kaposi's sarcoma (10.4%), Squamous cell carcinoma (8.4%) and basal cell carcinoma (7.8%) (1,2,19). Other non-melanoma skin cancers are not well documented in Tanzania. On the other hand, Cancer Registries in Uganda and Zimbabwe have reported increased prevalence of KS. The commonest risk factors for skin cancer are genetic predisposition, especially Albinism; followed by immunosuppression (1,2).

Primary Malignant skin conditions are generally classified in to two categories; the Non melanoma Skin Cancer (NMSC) and the Malignant Melanoma (MM). The Non melanoma skin cancers include Squamous Cell Carcinoma (SCC) and Basal Cell Carcinoma (BCC). Furthermore, Kaposi's sarcoma (KS) is an angio proliferative disorder that requires infection with Human Herpes Virus 8 (HHV-8), also known as Kaposi sarcoma-associated herpes virus (KSHV). It is one of the skin malignancies manifested mostly in immunocompromised individuals with late stage of AIDS. It is the second most common cancer in Tanzania, following the leading skin cancer which is melanoma (2,14).

There are several known causes and risk factors for acquiring skin cancer. Ultraviolet radiation (UV-light) is the most common cause of skin cancer (4,14,15). The probability

of developing skin cancers from UV-light exposure goes hand in hand with the amount and duration of UV-light exposure. There are mainly two mechanisms in relation to UV-light exposure resulting in to skin cancers. Firstly, UV light exposure causes skin cancers by a direct damage to the DNA molecule, which leads to mutations on subsequent cell cycle. Secondly, the mutations can occur in the host immune cells and can thus reduce their ability to remove malignant cells. Majority of squamous cell carcinomas have UV induced p53 mutations, which lead to uncontrolled over proliferation of keratinocytes. In melanoma there is a DNA mutation in the Cyclin-dependent kinase inhibitor-2A (CDKI-2A), and also the DNA repair enzymes have been found to contain mutated p53 genes and also melanocytic receptors 1 (MRCR1) (14). Chronically inflamed ulcers has also been reported to change to malignancies during prolonged exposure to UV-light and inflammation process (16).

1.1.1 Treatment Modalities for skin cancers.

Based on the status of lesions, whether premalignant or solitary malignant lesions, a variety of local and systemic interventions can be done. These include Cryotherapy and wide local excision followed by chemotherapy. In recurrent or aggressive forms, which are not good candidates for local therapy, radiation therapy and systemic medications are preferable(19). Furthermore, there are some advanced methods in molecular biology technology in treating skin malignancies as reported by Chinese Journal of Chemistry which gives hope for the future treatment and cure for skin cancer (21). This encompasses advanced chemotherapy and immunotherapy aimed at the molecular level by altering the immune system to recognize and target specific cancer cells and induces apoptosis (2).

1.2 Problem statement.

According to the 2020 cancer registry statistics, skin cancer is a major public health burden worldwide with malignant melanoma being the 17^{th} commonest cancer in the world, whereby 150,000 new cases occurred in 2020 alone. From the study done on Global burden of Skin Cancers it was reported that there is a 20-year projection of a 50%

increase in the burden of skin cancer (3). Hence it is important to have current data on pattern, prevalence, and clinical presentation of malignant skin lesions in Tanzania.
The country has witnessed efforts to improve the control of cancers generally, that also include skin cancers. However, there are still challenges related to late diagnosis and availability of optimal treatment.

It can thus be summarized that there is a gap in Tanzania of current data on pattern, clinical presentation, outcome of treatment following currently available treatment modalities, and factors that may affect the outcomes. This dissertation sought to address this gap.

1.3 Conceptual frame work

Individuals in Tanzania who are at risk will develop skin cancer with variable clinical presentation in terms of the type of skin cancer and also in terms of the distribution of the lesions on the patients' skin and the body. Available treatment options in the country can offer significant improvements. However, timely access to these interventions can be affected by a number of personal, societal and institutional factors that may eventually determine the success and outcomes of such interventions.

This is summarized in the figure below which incorporates both dependent and independent factors.

***Independent factors*;** These are non-modifiable risk factors for example albinism, Baseline investigations such as hemoglobin and staging of skin cancer at diagnosis Duration of symptoms onset and delay in primary care to referral for biopsy and definitive treatment institution, histopathological type of cancer, metastases, age, socio-demographic characteristics, and comorbidities at presentation**.**

***Dependent factors (modifiable factors*);** Types and choice of skin cancer treatment, treatment outcome for example healing of the ulcer, time to remission of symptoms, clearance of cancer cells, cure rate and survival time. Chemotherapy and radiotherapy

side effects such as anemia, weight gain or weight loss causes of recurrent admissions, are inclusive in this category.

Exposure to risk factors leads to development of malignant or premalignant lesions; a good clinical and histopathological diagnosis, early referral to capable centers is key to early choice of treatment modality and affects the outcome of treatment despite presence of comorbidities if at all.

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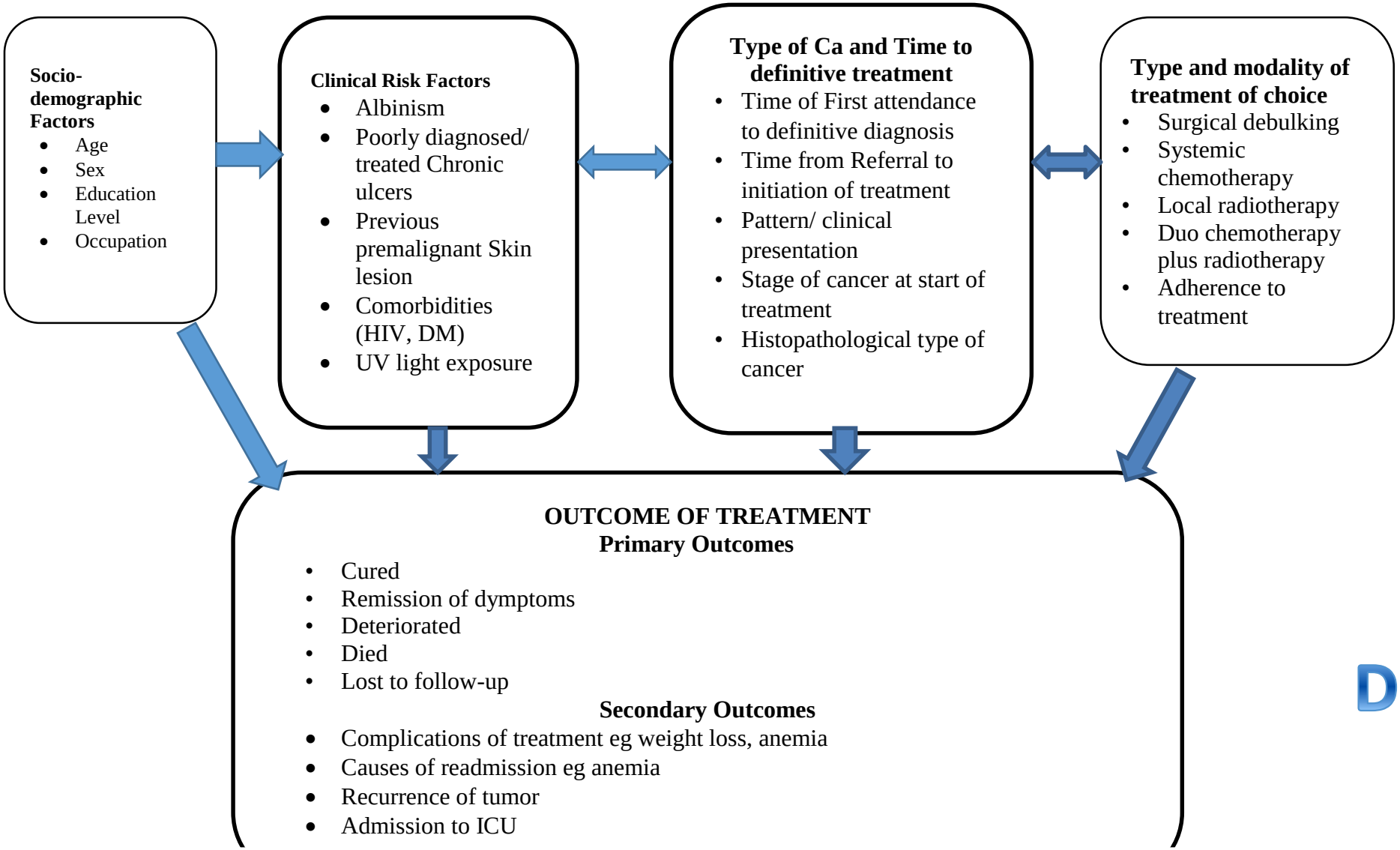


Figure 1: Conceptual frame work summarizing the inter-relationship between independent factors and dependent factors

1.4 Rationale

This study aims at providing the current picture on the pattern, prevalence and presentation of skin malignancies among adults in Tanzania and also providing information on the time interval between onset of symptoms to referral for treatment at the tertiary health care facilities. It also describes the factors associated with outcomes following provision of available treatment modalities.

This study will help health care givers, health care system, stake holders and the society on the importance of early detection, presentation and timely referral for diagnosis and better treatment options for good outcome of skin cancers.

The health care system will benefit and the burden will be reduced at ORCI as many patients will be diagnosed and referred earlier for treatment. The society will benefit as mortality and morbidity from skin cancer will be decreased, and the overall economic burden of skin cancer also improved if early intervention is adopted.

Also, findings from this study may be used by the Ministry of Health to develop appropriate health policies and strategies to fight against skin cancer.

1.5 Research questions.

1.5.1 Overall research question:

What is the prevalence and the pattern of skin cancers which are seen at the ORCI, and how do these present clinically? Additionally, what is the duration from onset of symptoms to definitive diagnosis and initiation of treatment; and what are the outcomes of currently employed treatment modalities, as well as the factors which influence such outcomes?

1.5.2 Specific research questions:

The following specific questions guided this research work:

i. What is the prevalence and pattern of histologically confirmed skin cancers among patients attended at the ORCI?
ii. What are the clinical manifestations of the common skin cancers seen at the ORCI?
iii. Among patients with skin cancer seen at the ORCI, what is the average time it takes from onset of symptoms to initiation of treatment?
iv. What are the outcomes of treatment for skin cancers being offered at the ORCI?
v. What are the factors that are associated with the outcomes among patients with skin malignancies attended at the ORCI?

1.6 Study Objectives

1.6.1 Broad Objective.

To describe the pattern, clinical presentation, time interval from presentation to definitive diagnosis and definitive treatment, treatment outcomes and their associated factors among patients with skin cancers treated at the Ocean Road Cancer Institute (ORCI) in Dar Es Salaam, Tanzania.

1.6.2 Specific Objectives

i. To determine the prevalence and pattern of histopathologically confirmed skin cancers attended at the ORCI
ii. To describe the clinical presentation of skin cancers being attended at the ORCI
iii. To assess the time interval from symptoms onset to initiation of treatment at ORCI among patients with skin cancers.
iv. To document the modality of treatment and determine the outcomes of treatment of choice provided to patients with skin cancer at the ORCI.
v. To determine the factors associated with treatment outcomes among patients with skin cancers attended at the ORCI

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 General overview of skin cancer

The WHO has reported that there are about 300,000 new cases of skin cancer, with approximately 1 million new cases of Keratinocyte Carcinomas(2). The reported numbers are likely to be low due to challenges related to diagnosis, reporting and data record keeping in oncology settings (1,2)

In the US the mortality from skin cancers was estimated to be 4,360 deaths per year 2021(12). In Southern Africa data on the epidemiology of skin cancers and the public health strategies employed for prevention of skin cancers were determined in 2020 and incorporated data registries from 5 countries. It was found that South Africa had the highest rate of both Cutaneous Melanoma and Keratinocyte Malignancies, with an increase of 103,351 cases between 2010 and 2014. Swaziland had a lowest rate of 93 reported cases and Botswana had 442 reported cases. In this study both limitations of data collection resulted from inadequate or poor cancer registry and tracking of patients. South Africa however had a better provision of extensive medical care and society awareness despite having a higher population of fair skinned population compared to other southern African countries, which might be the reason for a higher incidence in South Africa(3,4).

In Tanzania skin cancers had reached an incidence of 343 reported cases, or 0.09% of total deaths as per the WHO's published data of 2018. The incidence and mortality from cancers are higher among females compared to males; with the incidence in females being 1.8 times more compared to males, and a mortality of 1.3 times higher in females compared to 0.9 in males (1,2)

Skin cancer ulcers can mimic various ulcers, for example venous ulcers. Several studies and case reports have reported that some chronic ulcers from various causes like venous ulcers, burn, trauma and diabetic foot ulcers can develop into malignant skin lesions.

Pressure sores are the least ulcers to turn into cancer of which only 0.5% can develop into cancer. Most skin ulcers changes to squamous cell carcinoma and basal cell carcinoma. Symptoms of an ulcer which changes into cancer include excessive granulation at the base of an ulcer, margin changes, severe pain and bleeding which were previously minimal. (15,19,29)

Of the reported Skin cancers in Tanzania, Kaposi's sarcoma (KS) has been reported to be the commonest, with a prevalence of 7% in Tanzania. There are three categories of Kaposi Sarcoma; AIDS related Kaposi Sarcoma, Classic Kaposi Sarcoma occurring in the elderly without HIV infection and Endemic Kaposi Sarcoma prevalent in sub–Saharan Africa. The etiology of Kaposi Sarcoma is Human Herpes Virus-8 which induces cellular changes and enables the virus to evade the host immunity system and infect cells causing them to proliferate uncontrollably. It is transmitted through body fluids such as saliva during childhood, the virus infection compounded with AIDS proliferate malignant cells (14). Treatment of KS is related to suppressing the HIV virus with antiretroviral drugs which suppresses proliferation of KS cells hence regression. Further treatment can be warranted in advanced stage in which chemotherapy is the main treatment modality (19, 23).

2.2 Pattern, prevalence and clinical presentation of skin cancers.

Skin cancers are fairly common. A study conducted by world cancer statistics in the year 2022 noted that Dermatological cancers comprised of 17th commonest cancer with a prevalence of 12.7 of all malignancies (1,6).

They are frequently located on the sun-exposed areas of the body, particularly the head and neck regions as well as extremities, and can result in severe morbidity as posing difficulties in treatment through surgery and radiotherapy depending on the site, tumor extent of invasion and presence of metastases

Although most studies have shown that most skin cancers occur in males, a study conducted in northern Tanzania in the year 2012 found a female predominance of skin

malignancies among albinos (52.6%). Furthermore, this study found that the most common skin cancer was malignant melanoma (67.5%) followed by Kaposi's sarcoma (10.4%), squamous cell carcinoma (8.4%) and basal cell carcinoma (7.8%). The types of malignant melanomas were nodular malignant melanoma (37.5%), superficial spreading malignant melanoma (27%), while 8.1% were Amelanotic malignant melanoma (23). Lower limb was the most common site for skin cancer in which the study done concluded that two third of squamous cell carcinoma were in the lower limbs and were secondary to chronic leg ulcers (13, 19, 24)

Similar findings have been reported from a study done in Togo in 2021 on factors associated with skin malignancies in people with albinism. It was found that there was a slight female predominance with a male to female ration of 0.9. Basal cell carcinoma was dominating and the most affected areas were cephalic region (56.2%) followed by upper limbs (24.1%). The mean age was 39 years and some patients had multiple lesions ranging from one to 10 in one patient. In this study UV light protection knowledge and practices together with advanced hospital care were some of the factors influencing the results as many were in the rural areas which implied poor early health seeking as they couldn't afford to come to a tertiary hospital for checkup (25)

In the US Basal cell carcinoma is the most common type of non-melanoma skin cancer 80% of skin cancer most common in Hispanic and Asian races and can present with skin pigmentation in more than 50% of cases (2). They can be asymptomatic papules or nodules, which can have translucent central ulceration. In Saudi Arabia a systematic review done by Mohammad et al in 2020 on epidemiological patterns of skin diseases also concluded a higher prevalence of Basal Cell Carcinoma 51.4% followed by Squamous Cell Carcinoma 22.5 %, whereas malignant melanoma represented only 3.8% of the malignant skin disease spectrum (9).

Similarly, in the year 2010 a study conducted in Manipur India which was a review of 125 histologically diagnosed skin cancers, found that squamous cell carcinoma was the most common, accounting for 40% of all skin cancers, followed by melanoma which

accounted for 34% of skin cancers. It was also noted that skin cancers were most prevalent in the 6th and 7th decades of life. Malignant Melanoma was the most lethal skin cancer accounting for more than 1/3 (79%) of skin cancer deaths. The major prognostic determinant of this deadly neoplasm being the depth of invasion. On the other hand, Kaposi's sarcoma was the 4th most prevalent, accounting for 8% of the skin cancers (8,25–27).

It has also been reported that Squamous cell carcinoma presents approximately 20% of all skin cancers and is the second most type of cancer in Hispanic and Asian women in the US (2). It can present with scaling, indurated well circumscribed papule or plaque with ill defined, rough, pink patches which can bleed, ulcerate or present as chronic non healing ulcers or scars (1,26,27). On the other hand, Malignant Melanoma carries the highest mortality in patients of colour and can present as irregularly shaped dark macule or patch arising from pigmented nevi. This cancer can metastasize early and spread to other regions (13,27).

In the tropics, Skin cancer is one of the major causes of morbidity among albinos. Although Skin cancers are commonly seen in middle aged and elderly individuals, among the albinos the skin cancers present earlier. In a study conducted in Kenya in 2017 it was found that the rate of skin malignancies was 13.24 percent for skin cancer and 54.96 percent for cutaneous pre malignancy. Majority of patients in this study were aged between 21 and 30 years (28).

Pre-existing cutaneous disorders can also predispose to development of skin cancer. Squamous cell carcinoma has been reported in patients who had chronic leg ulcers and burn scars of which most patients are taken care of in peripheral health care facility (29). On the other hand, among albinos premalignant and malignant conditions such as actinic-cheilitis, solar elastosis and actinic keratosis have been found to predispose to later development of skin cancer. The prevalence of actinic Keratosis and actinic-cheilitis were found to be 37% and 17.9% respectively among Albinos The most common anatomical distributions were on the face and shoulders and hands for both conditions.(28)

Studies done in Manipur India, Togo and Northern Tanzania reported that the commonest site of cancer involvement among albinism was the head, especially the face and neck with much involvement of sun exposed areas. In these studies the mean ages at diagnosis were different; being 70 years in Manipur and 30 years in Tanzania, and there was a slightly more female prevalence. These differences were accounted for albinism, because in Tanzania the retrospective study recruited only people with albinism which is the same as in the study done in Togo (6, 25).

2.3 Risk factors in relation to Development of skin malignancies.

The exact cause of skin cancer remains unknown. However, important factors that have been strongly correlated with development of skin cancer include age, male sex, genetics, immunodeficiency, and ultra-violet (UV) radiation. There is still knowledge deficit on the risk of developing skin cancer from UV radiation exposure. This is exemplified by a study done in south Africa on UV-induced skin cancer knowledge and sun exposure preventive behavior among university students which pointed out a further need for knowledge and further investigations (3). Immunodeficiency secondary to HIV infection has been reported to account for half of the patients with Kaposi sarcoma (1, 2). Additionally, although skin cancers are known to develop in different age groups, they are relatively rare in the first decade of life but common in the 6^{th} and 7^{th} decades of life (9). Clinical suspicion and Physician's decision also have an impact on the definitive diagnosis, in a study done in South Africa the biopsied suspected skin lesions yielded a 68% of malignant lesions with basal cell carcinoma being the highest followed by squamous cell carcinoma (4).

Sun exposure remains one of the important risk factors in both white and black ethnicity.The risk in black population is not negligible, hence well informed interventions and knowledge among young adults is very important as illustrated in a study done in 2021 on the effectiveness of sun protection interventions delivered to adolescents (17). Knowledge and practices of using sun protection creams and limiting time of exposure are of paramount importance to avert this risk. In a cross-sectional study done in South

Africa only half of respondents of fair race reported regular use of sunscreen protection creams. In this study fewer had checked their skin for suspicious moles or lesions. It reported that only 30% of black ethnicity had knowledge of requirement and use of sunscreen to limit amount and time of exposure (3,4). This implies a high risk for development of cancer in both races. Furthermore, it is known that Actinic keratosis is a common skin condition among patients with albinism and without treatment it progresses to squamous cell carcinoma. Early intervention to any lesion on hands or sun exposure areas among albinism patients provides prevention from progression to malignant lesions (4,5,30)

There is similar risk on development of Basal Cell Carcinoma in both males and females. In a study done in 2019 to assess whether the male sex was an inherent risk factor for basal cell carcinoma it was found out that indeed both sexes had similar risk for the malignancy, although there was a bi-modal incidence rates and males had a higher rate of BCC development at older age. This was presumably due to genetic differences in oxidative stress, gene expressions as well as differences and preferential tanning behavior in younger females. (29)

2.4 Duration of symptom onset to diagnosis and treatment

Delays in seeking and being offered appropriate care for skin cancers remains a serious challenge, especially in developing countries like Tanzania. It has been reported that the duration of illness at diagnosis varied from 1 month to 60 months from the onset of symptoms and referral to tertiary hospitals with advanced diagnostics and treatment options according to guidelines was quite delayed. Most of the patients received interventions in peripheral dispensaries. These interventions delayed accurate diagnosis and initiation of available treatment options at the Ocean Road Cancer Institute and they presented with advanced cancer (8, 22, 29).

In a study done among people with albinism in northwestern Tanzania; most were sick for almost 2 years before presentation at tertiary oncology hospital. Together with delays in starting treatment some had dropped out from further treatment and follow-up. Most

patients had undergone surgical excision as the modality of treatment together with other modalities but only 67% remained available for follow-up at 6 and 12 months. The reasons for loss to follow-up were not clearly stated but for late presentation the purported reasons were financial constraints and some had started treatment in traditional healer's clinics leading to prolonged delay in primary health care facilities (8, 22).

The outcome of treatment with available modalities can be impressive. In a study done in Congo with a mean time of follow-up of 5.7 months 90% percent of patients had clearance of tumors (6). Also, in a study done on Basosquamous carcinoma (BSC) and treatment protocols in 2018 by Jordan et al it was revealed that a good recovery could be achieved with wide local excision as the tumors were diagnosed early and surgery was performed early, although it is also known that BSC have generally a low metastatic and recurrence rate. In this review there were no cases of local recurrence after surgery or metastatic disease or referrals after discharge (25). This adds value for advocacy of early diagnosis and treatment. The recovery and outcome of different treatment modalities employed in Tanzania are yet to be determined as recently there have been improved centers for skin cancer diagnosis and treatment.

2.5 Referral time interval and reasons for delay of treatment

Delays in arrival for primary hospital care and the time interval from referral to arrival in tertiary hospital for treatment is also long for patients with skin malignancies because the referral system and economic burden is the same in both patients with signs and symptoms pertaining to cancer as also noted in a study done by Mabula et al (8)

According to a survey done in 2017 by WHO about 90 per cent of all patients with cancer arrive late at tertiary hospital for definitive treatment; this implies a similar picture about skin cancer whose cure rate is well established if treated early. Despite the core treatment of cancer in Africa being mostly donor-funded and hence some medications are given free of charge, still the economic burden involved in preliminary evaluation and several visits in different hospitals with no improvement of symptoms and no definitive evaluations hampers the core process of cancer care in these patients (2,12,22).

Misdiagnosis of lesions can also contribute to poor outcomes. This may involve wrongly labeling lesions as chronic non-healing ulcers while these are actually premalignant lesions (15). It has also been reported in other parts of Africa that both social discrimination and low financial status can hinder provision of early care. A study done in DRC Congo by Inena et al in 2020 reported that 24 % of people with albinism had experienced discrimination from close contacts, while 67 % experienced discrimination from the society (22) In the study done recently in Tanzania by Makene et al on pathway to overall cancer care in Tanzania a significant delay since onset, diagnosis and starting of treatment were alarmingly found to negatively influence oncology care. Of the interviewed 62 cancer patients a final diagnosis since the onset of symptoms was made almost one year, 358 days later. This was mostly accounted for by poor socioeconomic status with much money being lost through the referral systems in place those with low education, low income and non-professional occupations experienced longer delays before diagnosis. Health system experiences contributed to these socially inequitable delays. Many patients had moved around the health system extensively, mainly through self-referral as symptoms worsened (31).

2.6 Treatment modalities and response to treatment of Skin Cancers.

Based on the status of lesions, whether premalignant or solitary malignant a variety of local interventions can be done. These include Cryotherapy and wide local excision followed by chemotherapy. If the patient has multiple lesions or diffuse actinic damage, sensitization of the skin by topical agents such as 5-fluorouracil can be done followed by directed radiotherapy. If the tumor is located in sensitive areas like the face and are more than 2 cm in diameter then micrographic surgery can be done. In recurrent or aggressive forms, which are not good candidates for local therapy, radiation therapy and systemic medications are preferable. An example is the use of Vismodegin in basal cell carcinoma. A report from the American Academy of Dermatology shows a 99% cure rate for malignant melanoma which is detected earlier and has not spread to lymph nodes.

In Tanzania, Radiotherapy and chemotherapy are provided at the ORCI, with the MNH also playing the role through provision of surgery in the form of wide local excision or debunking surgery. In a study done by Potenza C et al in 2018 who analyzed literature of surgical and non-surgical treatment of invasive squamous cell carcinoma, it was found that surgery remained a gold standard of therapy followed by plastic reconstruction surgery, Moh's micrograph surgery and electrocautery or curettage. Radiation therapy and chemotherapy were best adjuvants for high-risk tumors of the head and neck. Chemotherapy was mostly reserved and useful in patients with advanced tumors which were non operable or those which had metastases (19).

There are some advanced methods in molecular biology technology in treating skin malignancies as reported by Chinese Journal of Chemistry which gives hope for the future treatment and cure for skin cancer (21). This encompasses advanced chemotherapy and immunotherapy aimed at the molecular level by altering the immune system to recognize and target specific cancer cells and induces apoptosis. An example is *Tisagenlecleucel* which according to the WHO was approved by the FDA in 2018 to be used in skin cancer treatment (2).

The response of treatment of skin cancer has been studied in relation to the histopathological types and stage of the cancer at initiation of treatment. Advances in treatment modalities have resulted into improved responses and outcomes of treatment including remission with tumor free margins and low rates of recurrence.

The deadliest skin cancer is malignant melanoma which has the highest potential to spread to other organs in the body. This cancer can be treated if diagnosed early. According to WHO the survival rate of melanoma in situ which is diagnosed early is 99% and the overall death rate of melanoma is 2.5 per 100,000 with lowest death rates among Asian or Pacific Islander females which is 0.3 per 100,000 individuals (1, 2).

Tumor excision with tumor free margins histologically confirmed is primarily the recommended and first-line treatment for primary melanoma of any thickness, as well as

for melanoma in situ. Extent of surgical margins should be based on tumor thickness. For patients with unresectable and metastatic melanoma, chemotherapy using Nivolumab plus Ipilimumab is the recommended treatment (18, 19).

Squamous cell carcinoma (SCC) is more aggressive than BCC and has a large potential of invasiveness and metastasis. The SCC in situ (Bowen's disease) is the least complicated in terms of management compared to the high-risk SCC, in which high complete response rates have been achieved by photodynamic therapy. On the other hand, localized SCC lesions are curable with local excision, radiation therapy, cryosurgery, and curettage. However, data from available clinical trials have not concluded on the superiority of local excision to local excision or therapy combined with adjuvant chemotherapy or immunotherapy (18, 21, 29)

For localized BCC lesion surgical excision, Moh's surgery or Cryosurgery and later combined with radiotherapy and chemotherapy like topical fluorouracil 5% are the options. The application has proved successful with recurrence free rates of up to 85-90% (18, 21). For metastatic lesions hedgehog pathway inhibitors like Vismodebig are used in patients who cannot benefit from excision and radiotherapy. Recurrence rate of BCC is low and most studies analyzed recurrence rate rather than mortality rate which is reported to be 18% in 5 years. However, in metastases mostly chemotherapy is the treatment of choice (14, 18, 21, and 31).

Unfortunately, in Tanzania the availability and choices of different treatment modalities including newer generations of chemotherapy and their efficacy are yet to be determined.

2.7 Survival rate of skin cancers

The survival rate of skin cancers varies according to histopathological type of the cancer, severity of the disease and comorbid conditions. From time of onset to definitive treatment initiation contributes to the outcome of treatment reflecting recurrence rate and mortality. It can be further individualized due to specific comorbidities of the patient, and complications during treatment such as anemia (14, 19, 21). The survival rate of skin

cancer in black patients is lower than that in whites. There are few data on survival rates in our setting and sub-Saharan Africa in general. In 2019 US statistics report on cancer reports that the 5-year survival rate from 2011 to 2015 for black patients was 66% compared with 90% non-Hispanic white patients. This can be attributed to late diagnosis in black patients compared to whites. The pattern of melanoma in black patients presents as acral lentiginous melanoma mostly on palms, soles of feet and beneath the nails (12, 14). The five-year survival rate for patients with melanoma depends on the time to diagnosis and starting of treatment and stage of the cancer. If detected earlier before it spreads to lymph nodes, the survival rate is 99%. The five-year survival rate if there is nearby lymph nodes involvement is 68% compared to those in whom there is distant lymph nodes involved, which is 30 % (2). The 5-year relative survival for BCC is 100% and that of patients with SCC is slightly less reported to be 95%. The better survival in non-melanoma cancers is attributed to its low-grade nature and slow progression and there are many known treatments for non-melanoma cancers compared to melanoma and also less recurrence rates compared to melanoma (18, 19,23). The 5-year survival rates of HIV associated Kaposi's sarcoma is 10% to 30% while that of endemic Kaposi's sarcoma can be approximately 95% (1,12).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

A hospital based retrospective cohort study was carried out at the ORCI utilizing data and records of patients treated for skin cancer from **January 2019 to October 2023**. This study used patient data obtained from medical records as extracted from the institutional electronic database as well as the physical files that were available.

3.2 Study Duration

This study was conducted at ORCI utilizing records of patients who were treated in the previous five (5) years. During the study period piloting and pre-testing of data collection tools was done and then data of all patients who have been treated for the last 5 years (January 2019 to October 2023) were extracted from hospitals medical records and hospital data base for recruitment and analysis.

3.3 Study Site Study Population

This study was conducted on adult patients who were 18 years and above and received treatment at the Ocean Road Cancer Institute (ORCI) in Dar es Salaam. The ORCI is located in the heart of the Dar es Salaam central business district. It is Tanzania's oldest and most prominent cancer institute, renowned for delivering state-of-the-art radiotherapy and chemotherapy for malignancies. It proudly serves as a teaching hospital affiliated with the esteemed Muhimbili University of Health and Allied Sciences (MUHAS). The ORCI attends patients from all referral hospitals from the country. Up to 5000 patients with cancer are attended annually, of which approximately 165-175 patients have malignant skin conditions. Approximately 75 patients are admitted for treatment with advanced cancer or metastases of skin cancer.

The facility has an electronic database which started to operate on 2017, during the initial phase physical files were still being used for inpatients and all records in the wards. From 2019 the whole record system shifted to paperless mode in which both outpatient and

inpatient information were recorded on the computers system by the electronic software adopted at the institution. ORCI has wards for inpatients and runs outpatient clinics for both insured and public clients.

The study included adult patients treated at the ORCI for the last 5 years (January 2019 to October 2023). The total number of patients with skin cancer who were attended at the ORCI during this period was 877.

3.3.1 Skin cancer treatment in Tanzania

As noted above, in Tanzania the ORCI is equipped with treating modalities including adjuvant chemotherapy or radiotherapy depending on the stage of the cancer; while debulking surgeries are done in the peripheral regional hospitals or the MNH. Histology slides are prepared before the patient is sent to ORCI to start treatment. On the other hand, the KCMC has similar treatment modalities of chemotherapy and radiotherapy in the oncology unit which has been in operation for the past one year. At the BMC there is an Oncology unit too with similar treatment modalities as per current guidelines. Both of these centers lack some updated and advanced infrastructure in terms of means of providing radiotherapy and other diagnostic machines for metastases example PET scan which is only present at the ORCI.

3.4 Inclusion and Exclusion.

3.4.1 *Inclusion Criteria*

- **Adult patients aged 18 years and above**
- Histological proof of skin cancer
- Receiving treatment at the ORCI in form of radiotherapy, chemotherapy or both.
- Consent (verbal) over the phone from patients or patients' relatives for further interview about clarification on important information.

3.4.2 Exclusion Criteria

- Patients whose further information was needed but they did not provide informed verbal consent over the phone for further interview.

- Patients with records that are missing key data, for example staging of tumor at presentation, location and histopathological type and unknown outcome.

3.5 Sample Size Estimation.

The sample size for the study has been calculated using Cochrane formula**:**

$$n = \frac{Z^2 p (1-P)}{\varepsilon^2}$$

Whereby;

P is the chosen proportion of skin cancer in an oncology center (12.8%)

E=Margin of error/precision of 0.03(3%) for a P of 12.8%

N is the minimal sample size, and z is the standard normal deviate (1.96)

For this study a P = 12.8% has been chosen, being the proportion of patients with skin malignancies in Bugando Medical Centre in 2022. Among patients treated with malignancies 12.8% had skin malignancies (8).
Therefore,

$$n = \frac{1.96*1.96*0.128*(1-0.128)}{0.03*0.03}$$

n= 476

The total calculated Sample size was 476. To account for losses this was upped to 480.

3.6 Sampling technique and study procedures

Systematic sampling was used, whereby every 3rd patient meeting study inclusion criteria and registered in the electronic database was enrolled until the sample size of 480 was reached. The selection of comprehensive medical records that contain the necessary data

for the study was done using a convenient sampling technique. Sampling biases were minimized by choosing all essential medical records within the required period. At ORCI patients' records have been recorded and saved in the Hospital electronic database. Physical files are also present for those patients who were attended in the wards in 2019 when the paperless system was not in full function.

Hence data was obtained from the hospital's electronic database and the patients' files in medical records. When necessary, further inquiry of certain missing information for example treatment outcome was sought from patients themselves and the next of kin through mobile phone communication by their phone numbers used during registration process. To facilitate this, phone numbers of both study participants as well as their next of kin as used during the registration process at the hospital were obtained.

A structured data collection tool was used for collecting data which included socio-demographic characteristics, comorbidities, stage of cancer at presentation, site, number of malignant lesions, treatment given and outcome after treatment. Pre-testing of the data collection tool and piloting was done; the tool have been reevaluated as to meet all the objectives in this research, and all factors were taken care of in a reliable and validated procedure.

3.7 Study variables

In this study, the following study variables were used:

3.7.1 Independent Variables

Age, sex, level of education, occupation, skin type for example albinism, history of previous skin lesions, number of times of clinic visits for treatment at peripheral level and other comorbidities at presentation (HIV, DM, HT, Heart failure, kidney failure), radiological findings from X-rays and/or CT-scans or ultrasound suggesting metastases, time from symptoms to diagnosis, modality of treatment offered, Histopathological diagnosis, Morphology and distribution of skin lesions, Staging cancer and baseline hemoglobin levels.

3.7.2 Dependent Variables

Dependent variables are several outcomes of treatment for patients treated according to their type and extent of cancer

Primary outcome: Treatment outcome (cured, deteriorated, died, lost to follow up),

Secondary outcomes: Causes of re-admission or recurrences of skin lesion, complications of treatment. For example, anemia, weight loss/gain, early readmission, and admission for intensive care of therapy for deteriorating patients.

3.8 Data Collection and Management

A specially designed data extraction tool was used for data collection. This was filled in by the Principal Investigator and two Trained Research Assistants. All required information was obtained and filled in to a pre-tested data extraction form with all variables included. The original data Collecting tool forms are stored securely. Electronic data was also stored securely on a password-protected laptop computer to which the researcher alone had access. Paper based questionnaire data will be retained for three years in case there is a need for reference or data cleaning before its disposal.

This tool was improved and integrated into the web-based Google form enabling data collection using portable electronic devices. Web based Google forms facilitate the synchronization, extraction, and transfer of collected data to the analysis software such as SPSS. In this case Google forms developed were used and later on exported to a Microsoft Excel sheet that was subsequently linked to SPSS. The Google forms provide better data retention in the Google drive's data saver and are only accessible by the Principal investigator.

The patient's saved information at the time of hospitalization were recorded on the data collection tool. The data collection tool was divided into the following sections; socio demographic characteristics, clinical characteristics, previous history of skin lesions (whether treated and cured or none), duration and type of symptoms until definitive diagnosis is made and treatment started, other comorbidities, physical examination findings including location, size and morphology of presenting skin lesions, and

histopathological and other lab results, treatment given, treatment outcome, time to remission of lesions or occurrence of new lesions or metastases or complete cure and discharge from the clinic.

Baseline characteristics of participants during arrival at hospital were also recorded with specific dates. Dates of treatment initiation and outcomes during follow-up clinic visits was obtained to get the duration of follow-up of individual participants from the time of arrival to hospital until completion of treatment and discharge from clinic or when the event of interest occurred, such as loss to follow-up or death. Also, all events that occurred during the period of treatment such as complication of treatment, deterioration of the condition, recurrence of cancer or metastases were recorded with the specific dates. At ORCI all patients are registered with their mobile phone numbers and next of kins' phone number during the registration process on arrival at medical records department. The patients contact and next of kins' contacts were available, recorded and used to obtain additional information necessary for those instances in which the patients' recorded information was insufficient or the outcome was not recorded. The progress and outcome of treatment also was obtained from the relatives for those patients who are still on treatment, have died whether due to cancer, complication of treatment or other causes. Other information which was missing in participants files was also obtained from the next of kin via mobile phone interviews. Pre-testing of the data collection tool was done before data collection to ensure validity and feasibility.

3.9 Data analysis

Statistical analysis was done using SPSS version 23.0. Descriptive analysis was used for both continuous and categorical data. Categorical variables such as sex, skin type, histological types of cancer, time intervals from symptoms to definitive treatment initiation were presented as frequencies and percentages. Continuous variables such as age were summarized using measures of central tendency as means (± standard deviation). Chi square test was used to compare if there was a statistically significant difference in proportions between groups for outcome. Multiple logistic regression was used to determine associations between independent variables for the outcomes of treatment of

choice of different stages of skin cancer. Before Multivariate analysis, a bivariate analysis was performed and variables with a p-value = 0.2 were entered into the multivariate analysis to determine associated risk factors for outcomes, for example death using odds ratio and 95% confidence interval. Kaplan Meir analysis was used to describe the one-year survival.

A p-value less than 0.05 was regarded as being statistically significant.

3.10 Validity and reliability

Study credibility was maintained through thoroughly testing and adjusting data collection tools to ensure reliable data collection methods during the whole process. Only trustworthy and comprehensive medical records were included in the study to maintain consistency and reliability. The leading researcher carefully reviewed all previously recorded information on staging, clinical presentation, treatment of choice and duration of treatment and follow up clinics documented. The Principal Investigator consulted the Oncologist at ORCI when uncertainties arose to ensure accurate documentation using pre-installed software on mobile devices streamlined data collection, reducing the chances of incorrect data entry and coding errors.

3.11 Pretesting and pilot data tools

The Principal Investigator conducted a preliminary study to improve the data collection instruments to be used in this research. This pilot study involved analyzing 40 patient data, representing ten per cent of the required sample size. The findings from the pilot study, specifically regarding data integrity, were thoroughly evaluated, and the tool was revised accordingly. The valuable insights gained from the pilot study were integrated into the research process which enhanced effectiveness and accuracy of the data collection process.

3.12 Ethical issues

Ethical clearance was obtained from the MUHAS Research Ethics Committee. Permission to conduct the study was obtained from the administration of ORCI and a

formal permission letter to collect data was issued. All protocol advised was followed and Waiver form for data collection was used at ORCI.

Patients and relatives who were sought by their mobile phone numbers were asked to consent on a verbatim basis over the phone to participate in the study and consenting ones were enrolled and further interviews conducted. Confidentiality of their information was maintained by not providing names of patients and strictly using the data for this research only. The data and information were anonymized in terms of names of patients interviewed over the phone.

3.13 Study findings and dissemination

Findings of this study have been presented at the Department of Internal Medicine. The final report will be available at MUHAS library. Findings will also be presented at scientific conferences and published in a peer-reviewed medical journal.

CHAPTER FOUR

4.0 RESULTS

4.1 Social demographic characteristics of participants at enrolled

The study enrolled 480 participants who attended the ORCI between January 2019 and October 2023, providing insights into their social demographic characteristics.

As shown in table 1, majority of participants were middle aged with a mean (±SD) age of 49.9 (15.7) years regarding gender distribution, majority were male (58.5%) and hence 41.5% were female. Age-wise, 29.0% were below 40 years old, 45.2% were aged between 40 and 59, and 25.8% were 60 years old and above. Occupation status varied among the participants, with majority (43.3%) being peasants and 18.8% participants were unemployed. Only 12.9% were formally employed and 19.0% were self-employed business owners. Education levels showed diversity, with lesser percentage of those attaining higher education levels; only 10.4% have completed college or university education, 21.7% having no formal education and majority (52.7%) had completed primary education.

In terms of marital status, majority (56.9%) of participants were married, 27.1% were single, and 11.3% were widowed which is also similar In every skin cancer category. The Monthly income distribution revealed that majority (32.9%) earned between TZS 50,000 and 100,000, and 22.3% earning between 100,000 and 500,000 per month. A minority of participants earned highly as 8.1% of the participants were earning between 500,00 and 1,000,000 per month.

Regarding characteristics of participants in each specific skin cancer type; Females were predominant in Squamous Cell Carcinoma,68.5% and Basal Cell Carcinoma53.3%. However, majority of participants were peasants who attained primary level of education and earned between 50,000 and 100,000 per month across both Skin Cancer types as shown in table 1 below.This comprehensive overview of the participants' demographics provides a foundation for understanding the varied backgrounds and characteristics of individuals seeking health care at ORCI during the specified period.

Table 1. Social demographic characteristics of all Study participants (N=480) and by Skin Cancer type.

Variable	Frequency (%)	KS=275	SCC=108	MM=82	BCC=15
Sex					
Female	199 (41.5%)	103(37.5%)	**74(68.5%)**	24(29.3%)	**8(53.3%)**
Male	**281(58.5%)**	**172(62.6%)**	34(31.5%)	**58(70.7%)**	7(46.7%)
Age group					
< 40	140 (29.0%)	95(34.6%)	30(27.8%)	15(18.3%)	3(20.0%)
40 to 59	**213 (45.2%)**	**133(48.4%)**	38(35.2%)	30(36.6%)	4(26.7%)
60 and above	127 (25.8%)	47(17.1%)	40(37.04%)	37(45.1%)	8(53.3%)
Mean Age	49.9 (SD15.7)				
Occupation status					
Formal Employment	62 (12.9%)	41(14.9%)	8(7.4%)	9(10.98%)	2(13.33%)
Peasant	**208 (43.3%)**	**120(43.6%)**	**72(66.7%)**	**43(52.4%)**	**6(40.0%)**
Self-Employed (Business Owner)	91 (19.0%)	65(23.6%)	15(13.9%)	8(9.8%)	3(20.0%)
Unemployed	90 (18.8%)	49(17.8%)	13(12.04%)	22(26.8%)	4(26.7%)
Education Level					
Primary	**253 (52.7%)**	**132(48.0%)**	**68(62.9%)**	**40(48.8%)**	**9(60%)**
Secondary	73 (15.2%)	47(17.1)	10(9.3%)	13(15.9%)	

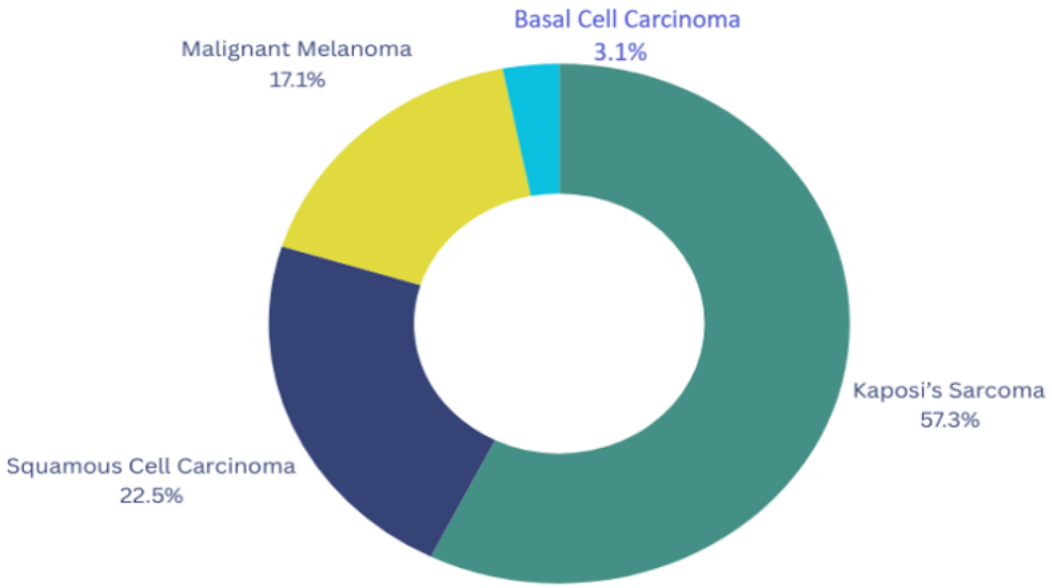
College/University	50 (10.4%)	38(13.8%)	5(4.6%)	9(10.9%)	2(13.3%)
No Education	104 (21.7%)	58(17.8%)	25(12.0%)	20(26.8%)	4(26.7%)
Marital status					
Married	**273 (56.9%)**	**154(56.0%)**	**60(55.6%)**	**53(64.6%)**	**7(46.7%)**
Single	130 (27.1%)	88(32.0%)	20(18.5%)	16(19.5%)	3(20.0%)
Divorced	23 (4.8%)	15(5.5%)	7(6.5%)	2(2.4%)	0
Widow	54 (11.3%)	18(6.6%)	21(19.4%)	11(13.4%)	5(33.3%0
Monthly Income (TZS)					
<50,000/=	27 (5.6%)	17(6.1%)	13(12.0%)	7(8.5%)	1(6.7%)
50,000/= 100,000/=	**158 (32.9%)**	**80(29%)**	**54(50%)**	**29(35.4%)**	**6(40%)**
100,000/= 500,000/=	107 (22.3%)	65(23.6%)	36(33.3%)	7(8.5%)	1(6.7%)
500,000/= 1,000,000/=	39 (8.1%)	26(9.5%)	5(4.6%)	6(7.3%)	7(46.7%)

4.2 Pattern, prevalence and presentation of skin malignancies.

4.2.1 Prevalence of histologically confirmed skin cancers

In this study Kaposi's Sarcoma was the most prevalent, accounting for 57% of cases (95% CI: 53% - 62%), followed by Squamous Cell Carcinoma at 22% (95% CI: 18% - 26%), and Malignant Melanoma at 17.1% (95% CI: 13% - 19%). Basal Cell Carcinoma constituted 3.1% of cases (95% CI: 1.7% - 5.2%). (Figure 2).

Figure 2. Pie chart Showing Prevalence of histologically confirmed skin cancers among patients attended at the Ocean Road Cancer Institute



4.2.2 Pattern of skin cancer lesions among patients attended at ORCI.

This overview of pattern delineates the varying distribution patterns of skin cancers based on lesion site on different parts of the body.

As shown in table 2b, at presentation to the ORCI, Kaposi's Sarcoma (N = 275) predominantly manifested on the lower limbs (79.6%), and less in the upper limbs (6.9%). On the other hand, Squamous Cell Carcinoma (N = 108) was frequently located on the head and neck (30.6%) and lower limbs (42.6%).

Malignant Melanoma (N = 82) often appeared on lower limbs (63.4%) and head and neck (12.2%), while Basal Cell Carcinoma (N = 15) primarily occurred on the head and neck (26.7%), lower limbs (40.0%) and less on upper limbs (13.3%).

Table 2: Pattern and distribution of primary sites involved among patients attended.

Site of the lesion	**BCC N=15**	**KS N=275**	**MM N=82**	**SCC N=108**
Head & Neck	**4(26.7%)**	17(6.2%)	10(12.2%)	**33(30.6%)**
Upper limb	2(13.3%)	19(6.9%)	8(9.8%)	10(9.3%)
Trunk	1(6.7%)	3(1.1%)	0(0.0%)	6(5.6%)
Genitalia	0(0.0%)	9(3.3%)	4(4.9%)	7(6.5%)
Lower limb	**6(40.0%)**	**219(79.6%)**	**52(63.4%)**	**46(42.6%)**
Unspecified site	2(13.3%)	8(2.9%)	8(9.8%)	6(5.6%)

4.3 Clinical presentation of skin cancers.

The clinical characteristics or presentation of the different types of skin cancer differed from one cancer to another. These are as summarized in table 3a below. They cover morphological aspects like lesion shape, colour, and surface area of lesions.

Kaposi's Sarcoma presented most frequently with irregular multiple nodular lesions in (36%), commonly hyperpigmented (47.3%), and most had an irregular nodulated surface (21.5%).

Squamous Cell Carcinoma presented with irregular-shaped lesions (39.8%) that were frequently black and reddish in colour (29.6% and 25.9% respectively).

Malignant Melanoma was characterized mostly by irregular and roundish lesions (39 % and 31.7% respectively), also most lesions were black (48.8%), while Basal Cell Carcinoma presented mostly with irregularly-shaped lesions which were mostly black in colour (66.7% and 46.7% respectively).

Further information with regards to a detailed description of the different types of skin cancers, the frequencies of description and number of patients who were examined, and clinical characteristics such as lesion shape, margin and surface are presented in Table 3a and Table 3b.

Table 3a: Clinical characteristics of skin cancers based on shape of the lesion

Shape of the lesion	**BCC N=15**	**KS N=275**	**MM N=82**	**SCC N=108**
Round	0 (0.0%)	67(24.4%)	**36(43.9%)**	29(26.9%)
Irregular	**10 (66.7%)**	**99(36.0%)**	32(39.0%)	**43(39.8%)**
Not Specified/ Documented	5 (33.3%)	109(39.6%)	14(17.1%)	36(33.3%)

Table 3b: Clinical characteristics of different malignant lesions based on surface and margin of the lesion.

Surface and margin	BCC N=15	KS N=275	MM N=82	SCC N=108
Regular margin	0 (0.0%)	0 (0.0%)	3(3.7%)	1 (0.9%)
Irregular Unraised Margin	7 (46.7%)	103 (37.5%)	15(18.3%)	22 (20.4%)
Irregular Raised Margin	0 (0.0%)	30 (10.9%)	21(25.6%)	35 (32.4%)
Ulcerated Surface	1 (6.7%)	3 (1.1%)	5 (6.1%)	6 (5.6%)
Fungating surface	2 (13.3%)	2 (0.7%)	14 (17.1%)	18 (16.6%)
Irregular and nodulated surface	2 (13.3%)	59 (21.5%)	8 (9.8%)	0 (0.0%)
Not Documented	3 (20.0%)	78 (28.4%)	14 (17.4%)	26 (24.1%)

4.4 Time interval from symptoms onset to receiving cancer treatment at the ORCI

Table 4 below shows the categorization of median time from symptom onset to presentation at the ORCI for the different skin cancers. Overall, the large proportion of patients diagnosed as skin cancer took 6 months from symptom onset to starting treatment. The percentage of patients with Kaposi's sarcoma who presented early for treatment (in less than 3 months) was 55.3%. In comparison to other categories, most patients had attended ORCI in three to six months period. Patients with basal cell carcinoma (40.0%), malignant melanoma (63.4%) and squamous cell carcinoma (58.3%) had moderate delay periods of three to six months respectively. 12.9% of patients with Squamous Cell Carcinoma had delayed for more than six months to attend ORCI for treatment as shown in Table 4.

Table 4: Duration of time since symptoms onset until institution of treatment at ORCI

Duration from symptom onset to receiving treatment (months)	Basal Cell Carcinoma, N = 15	Kaposi's Sarcoma, N = 275	Malignant Melanoma, N = 82	Squamous Cell Carcinoma, N = 108
Early (<=3 months)	5 (33.3%)	**152 (55.3%)**	21 (25.6%)	31 (28.7%)
4 to 6 (moderate delay)	**6 (40.0%)**	98 (35.6%)	**52 (63.4%)**	**63 (58.3%)**
>/= 6 months (severe delay)	4(26.7%)	25 (9.1%)	9 (11.0%)	14 (12.9%)

4.4 Outcome of cancer treatment

Outcomes of cancer treatment among patients is being presented based on the treatment modalities used and the duration of treatment. Survival was analyzed after 1 year of treatment.

Regarding treatment modality, the majority (79 out of 124) of patients who were cured received radiotherapy, followed by chemotherapy 42 out of 124 patients. Among the deceased patients, 25 out of 54 received chemotherapy, while 29 out of 54 received radiotherapy as shown in Table 5a below. Among the deceased patients, most (66.7%) had symptoms for a duration that ranged from 4 to 6 months before receiving treatment. Similarly, 47.8% of all patients who were still on treatment had a duration of symptoms of 4 to 6 months before initiating therapy at the ORCI. On the other hand, 19 patients (10.2%) had symptoms for more than 6 months. Among HIV patients with Kaposi Sarcoma; 30 were cured which accounts for 27.3%., while 16 (15.5%) died during treatment.

Regarding the treatment outcomes for both types of skin cancer, the majority of patients were treated with radiotherapy, as shown in Tables 5bi through 5biv. Among patients

with Kaposi's sarcoma still undergoing treatment, 85 out of 161 were receiving radiotherapy. Additionally, 44 out of 70 cured patients had received radiotherapy, as shown in Table 5 b i.

For patients with Squamous Cell Carcinoma (SCC) still undergoing treatment, 34 out of 63 were being treated with radiotherapy. Among those who were cured, 22 out of 32 had received radiotherapy, as shown in Table 5bii. 11 out of 13 Patients with Malignant Melanoma who were cured received radiotherapy and 5 out of 9 patients who died received chemotherapy as shown in table 5 b iii.

In contrast, all patients with Basal Cell Carcinoma (BCC) who were alive had received radiotherapy. Of the 7 patients still undergoing treatment, 3 received radiotherapy, and 3 received chemotherapy, as shown in Table 5 b iv.

Table 5a. Outcomes of cancer treatment among patients, focusing on the treatment modalities administered and the duration of treatment.

Variable	**Alive, N=124**	**Died, N=54**	**Still On Treatment, N=186**
Treatment Modality Given			
Both Radiotherapy and Chemotherapy	2 (1.6%)	0 (0.0%)	7 (3.8%)
Chemotherapy	42 (33.9%)	25 (46.3%)	86 (46.0%)
Radiotherapy	79 (63.7%)	29 (53.7%)	89 (47.8%)
Surgical Excision	1 (0.8%)	0 (0.0%)	4 (2.2%)
Duration of treatment			
<=3	27(21.8%)	11(20.4%)	78(41.9%)
4 to 6	87(70.2%)	36(66.7%)	89(47.8%)
6 and above	10(8.1%)	7(13.0%)	19(10.2%)

Tables 5b (i-iv). Outcomes of treatment among patients with skin cancers.

Table 5 b (i): Outcomes of treatment among patients with Kaposi's Sarcoma.

Variable	**Alive, N=70**	**Died, N=24**	**Still On Treatment, N=161**
Treatment Modality Given			
Both Radiotherapy and Chemotherapy	0	0	2(1.2%)
Chemotherapy	26(37.1%)	8(33.3%)	74(46.0%)
Radiotherapy	**44(62.9%)**	**16(66.7%)**	**85(52.8%)**
Surgical Excision	0	0	0

Table 5 b (ii): Outcomes of treatment among patients with Squamous Cell Carcinoma

Variable	**Alive, N=32**	**Died, N=18**	**Still On Treatment, N=63**
Treatment Modality Given			
Both Radiotherapy and Chemotherapy	2(6.3%)	0	1(1.6%)
Chemotherapy	8(25%)	**9(50.0%)**	**28(44.4%)**
Radiotherapy	**22(68.8%)**	**9(50.0%)**	34(53.97%)
Surgical Excision	0	0	0

Table 5 b (iii): Outcomes of treatment among patients Malignant Melanoma

Variable	**Alive, N=13**	**Died, N=9**	**Still On Treatment, N=37**
Treatment Modality Given			
Both Radiotherapy and Chemotherapy	0	0	1(2.7%)
Chemotherapy	1(7.7%)	**5(55.6%)**	15(40.5%)
Radiotherapy	**11(84.6%)**	4(44.4%)	**21(56.8%)**
Surgical Excision	1(7.7%)	0	0

Table 5 b (iv): Outcomes of treatment among patients with Basal Cell Carcinoma

Variable	**Alive, N=2**	**Died, N=0**	**Still On Treatment, N=7**
Treatment Modality Given			
Both Radiotherapy and Chemotherapy	0	0	0
Chemotherapy	0	0	**3(42.9%)**
Radiotherapy	**2(100%)**	0	**3(42.9%)**
Surgical Excision	0	0	1(14.3%)

5.1.1 Factors associated with outcomes of all skin cancer patients.

As shown in Table 6, on multinomial logistic regression, the only factor that was statistically significantly associated with a reduced probability of being cured was no education, with an AOR of 0.1 (95% CI of 0.01 to 0.88), and a p-value of 0.038.

The only factor was associated with a reduced probability of still being on treatment was also having no education, with an AOR of 0.07 (95% CI of 0.01 to 0.59), and a p-value of 0.015.

Other factors such as age group, duration of diagnosis, and insurance status did not significantly influence the outcomes.

Table 6. Factors determining patient outcomes among all patients with skin cancer.

	Alive		**Still On Treatment**	
Variable	**Adj Odds Ratios**	**p. Value**	**Adj Odds Ratios**	**p. Value**
Sex				
Female	1		1	
Male	0.89 (0.43 – 1.84)	0.747	0.92 (0.45 – 1.86)	0.812
Age group				
< 40	1		1	
40 to 59	0.86 (0.35 – 2.06)	0.728	0.83 (0.36 – 1.93)	0.659
60 and above	0.78 (0.30 – 2.03)	0.608	0.57 (0.23 – 1.44)	0.234
Duration of diagnosis (months)				
<4	1	1	1	1
4 to 5	1.35 (0.54 – 3.36)	0.524	0.48 (0.21 – 1.10)	0.081

6 and above	0.75 (0.20 – 2.81)	0.665	0.43 (0.13 – 1.44)	0.171
Education Level				
College/University	1		1	
No Education	0.1 (0.01 – 0.88)	0.038	0.07 (0.01 – 0.59)	0.015
Primary	0.13 (0.01 – 1.06)	0.057	0.19 (0.02 – 1.55)	0.12
Secondary	0.11 (0.01 – 1.11)	0.062	0.25 (0.03 – 2.35)	0.224
Insurance status				
Insured	1		1	
Not Insured	2.09 (0.85 – 5.11)	0.106	1.99 (0.85 – 4.68)	0.115
HIV Status				
HIV Positive	1.14 (0.26-5.13)	0.9	1.76 (0.5-6.6)	0.4
HIV Negative	1		1	
Marital status				
Married	3.29(0.15-74.6)	0.45	0.16(0.4-10)	0.2
Single	2.98(0.15-74.6)	0.45	1.7(0.12-24.7)	0.7
Divorced	-	-	-	-
Widow	1		1	

4.5.2 Factors determining outcomes of Treatment by type of skin cancer.

Factors associated with treatment outcomes were analyzed separately for each skin cancer type as shown in Tables 6a to 6d below. None of the factors that were entered into the regression model (age, sex, marital status, education level, insurance status, income, HIV infection and duration of symptoms) were associated with treatment outcomes for Kaposi sarcoma, Malignant melanoma, Basal cell carcinoma or Squamous cell carcinoma.

Table 6a: Factors determining treatment outcomes among patients with Kaposi's sarcoma.

	Alive		**Still on treatment**	
Variable	**Adj Odds Ratios**	**p. Value**	**Adj Odds Ratios**	**p. Value**
Sex				
Female	1		3.6 (0.7-17.5)	0.98
Male	1	1	1	1
Age group				
< 40	0.83 (0.36 – 1.93)	0.78	0.97 (0.145-6.56)	0.98
40 to 59	0.57 (0.23 – 1.44)	0.234	0.67 (0.95-5.18)	0.903
60 and above	1		1	1
Duration of diagnosis (months)				
<4	1	1	1	1
4 to 5	0.48(0.21 – 1.10)	0.081	1.3(0.2 – 8.5)	0.78
6 and above	0.43(0.13 – 1.44)	0.171	0.88(0.15 – 5.2)	0.9
Education Level				
Primary level	1.6(0.3-8.5	0.6	1.6(0.3-8.5)	0.6
Secondary Education	0.07(0.01 – 0.59)	0.4	4.9(0.4 – 8.5)	0.6
College/University	0.19(0.02 – 1.55)	0.12	4.9(0.3-87.7)	0.3
No Education	1	1	1	1
Insurance status				
Insured	0.7(0.1-3.6)	0.7	1	1
Not Insured	1	1	2.09(0.85 – 5.11)	0.106
Income				

<50,000	20.7(0.48-8.74)	0.113	4.0(0.1-1.12)	0.4
50,000-100,000	6,97(0.37-64.7)	1.19	3(0.3-35.4)	0.4
100,000-500,000	4.8(0.36-64.7)	0.23	1.9(0.2-17.6)	0.56
500,000-1,000,000	1	1	1	1
HIV Status				
HIV Positive	1.14(0.26-5.13)	0.9	1.76(0.5-6.6)	0.4
HIV Negative	1	1	1	1
Marital status				
Married	3.29(0.15-74.6)	0.45	0.16(0.4-10)	0.2
Single	2.98(0.15-74.6)	0.45	1.7(0.12-24.7)	0.7
Divorced	-	-	-	-
Widow	1	1	1	1

Table 6b: Factors determining treatment outcomes among patients with Malignant Melanoma

	Alive		**Still on treatment**	
Variable	**Adj Odds Ratios**	**p. Value**	**Variable**	**Adj Odds Ratios**
Sex			**Sex**	
Female	1		Female	1
Male	1.	1	Male	1.
Age group			**Age group**	
< 40	0.83(0.36 – 1.93)	0.78	< 40	0.83(0.36 – 1.93)
40 to 59	0.57(0.23 – 1.44)	0.234	40 to 59	0.57(0.23 – 1.44)
60 and above	1		60 and above	1
Duration of diagnosis (months)			**Duration of diagnosis (months)**	
<4	1	1	<4	1

4 to 5	0.48(0.21 – 1.10)	0.081	4 to 5	0.48(0.21 – 1.10)
6 and above	0.43(0.13 – 1.44)	0.171	6 and above	0.43(0.13 – 1.44)
Education Level			**Education Level**	
Primary level	1.6(0.3-8.5	0.6	Primary level	1.6(0.3-8.5
Secondary Education	0.07(0.01 – 0.59)	0.4	Secondary Education	0.07(0.01 – 0.59)
College/University	0.19(0.02 – 1.55)	0.12	College/University	0.19(0.02 – 1.55)
No Education	1	1	No Education	1
Insurance status			**Insurance status**	
Insured	0.7(0.1-3.6)	0.7	Insured	0.7(0.1-3.6)
Not Insured	1	1	Not Insured	1
Income			**Income**	
<50,000	20.7(0.48-8.74)	0.113	<50,000	20.7(0.48-8.74)
50,000-100,000	6,97(0.37-64.7)	1.19	50,000-100,000	6,97(0.37-64.7)
100,000-500,000	4.8(0.36-64.7)	0.23	100,000-500,000	4.8(0.36-64.7)
500,000-1,000,000	1	1	500,000-1,000,000	1
HIV Status			**HIV Status**	
HIV Positive	1.14(0.26-5.13)	0.9	HIV Positive	1.14(0.26-5.13)
HIV Negative	1	1	HIV Negative	1
Marital status			**Marital status**	
Married	3.29(0.15-74.6)	0.45	Married	3.29(0.15-74.6)
Single	2.98(0.15-74.6)	0.45	Single	2.98(0.15-74.6)
Divorced	-	-	Divorced	-
Widow	1	1	Widow	1

Table 6c: **Factors determining treatment outcomes among patients with Squamous cell carcinoma.**

Died (Reference)	**Alive**		**Still on treatment**	
Variable	**Adj Odds Ratios**	**p. Value**	**Variable**	**Adj Odds Ratios**
Sex			**Sex**	
Female	1		Female	1
Male	1.	1	Male	1.
Age group			**Age group**	
< 40	0.83(0.36 – 1.93)	0.78	< 40	0.83(0.36 – 1.93)
40 to 59	0.57(0.23 – 1.44)	0.234	40 to 59	0.57(0.23 – 1.44)
60 and above	1		60 and above	1
Duration of diagnosis (months)			**Duration of diagnosis (months)**	
<4	1	1	<4	1
4 to 5	0.48(0.21 – 1.10)	0.081	4 to 5	0.48(0.21 – 1.10)
6 and above	0.43(0.13 – 1.44)	0.171	6 and above	0.43(0.13 – 1.44)
Education Level			**Education Level**	
Primary level	1.6(0.3-8.5	0.6	Primary level	1.6(0.3-8.5
Secondary Education	0.07(0.01 – 0.59)	0.4	Secondary Education	0.07(0.01 – 0.59)
College/University	0.19(0.02 – 1.55)	0.12	College/University	0.19(0.02 – 1.55)
No Education	1	1	No Education	1
Insurance status			**Insurance status**	
Insured	0.7(0.1-3.6)	0.7	Insured	0.7(0.1-3.6)
Not Insured	1	1	Not Insured	1
Income			**Income**	
<50,000	20.7(0.48-8.74)	0.113	<50,000	20.7(0.48-8.74)

50,000-100,000	6,97(0.37-64.7)	1.19	50,000-100,000	6,97(0.37-64.7)
100,000-500,000	4.8(0.36-64.7)	0.23	100,000-500,000	4.8(0.36-64.7)
500,000-1,000,000	1	1	500,000-1,000,000	1
HIV Status			**HIV Status**	
HIV Positive	1.14(0.26-5.13)	0.9	HIV Positive	1.14(0.26-5.13)
HIV Negative	1	1	HIV Negative	1
Marital status			**Marital status**	
Married	3.29(0.15-74.6)	0.45	Married	3.29(0.15-74.6)
Single	2.98(0.15-74.6)	0.45	Single	2.98(0.15-74.6)
Divorced	-	-	Divorced	-
Widow	1	1	Widow	1

Table 6d: **Factors determining treatment outcomes among patients with Basal cell carcinoma.**

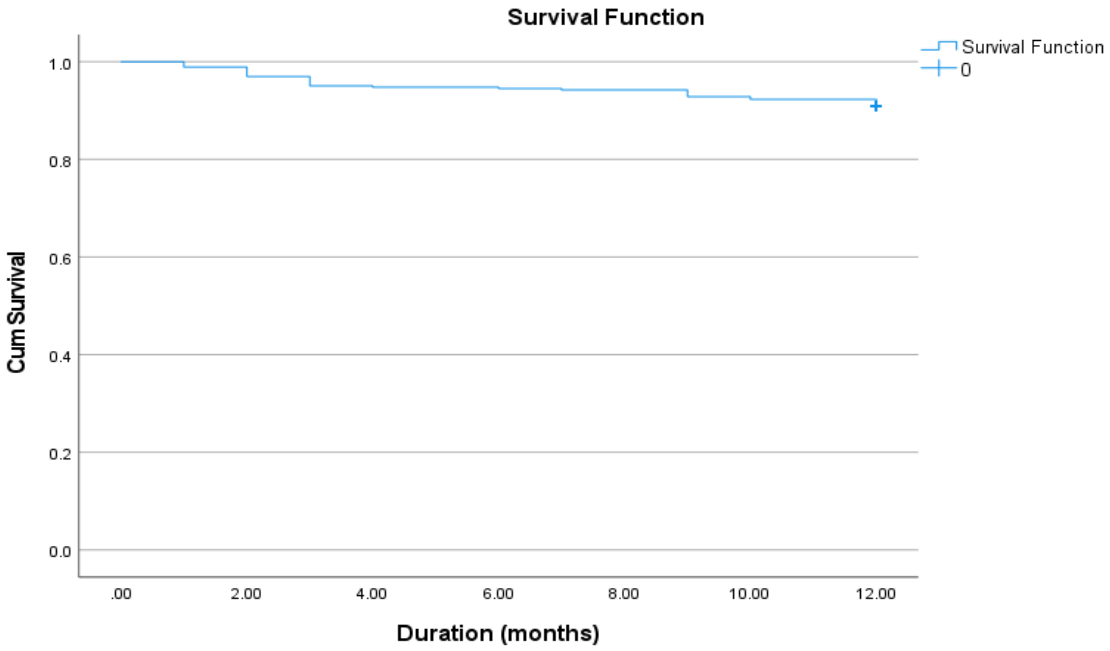
	Alive		**Still on treatment**	
Variable	**Adj Odds Ratios**	**p. Value**	**Variable**	**Adj Odds Ratios**
Sex			**Sex**	
Female	1		Female	1
Male	1.	1	Male	1.
Age group			**Age group**	
< 40	0.83(0.36 – 1.93)	0.78	< 40	0.83(0.36 – 1.93)
40 to 59	0.57(0.23 – 1.44)	0.234	40 to 59	0.57(0.23 – 1.44)
60 and above	1		60 and above	1
Duration of diagnosis (months)			**Duration of diagnosis (months)**	
<4	1	1	<4	1

4 to 5	0.48(0.21 – 1.10)	0.081	4 to 5	0.48(0.21 – 1.10)
6 and above	0.43(0.13 – 1.44)	0.171	6 and above	0.43(0.13 – 1.44)
Education Level			**Education Level**	
Primary level	1.6(0.3-8.5	0.6	Primary level	1.6(0.3-8.5
Secondary Education	0.07(0.01 – 0.59)	0.4	Secondary Education	0.07(0.01 – 0.59)
College/University	0.19(0.02 – 1.55)	0.12	College/University	0.19(0.02 – 1.55)
No Education	1	1	No Education	1
Insurance status			**Insurance status**	
Insured	0.7(0.1-3.6)	0.7	Insured	0.7(0.1-3.6)
Not Insured	1	1	Not Insured	1
Income			**Income**	
<50,000	20.7(0.48-8.74)	0.113	<50,000	20.7(0.48-8.74)
50,000-100,000	6,97(0.37-64.7)	1.19	50,000-100,000	6,97(0.37-64.7)
100,000-500,000	4.8(0.36-64.7)	0.23	100,000-500,000	4.8(0.36-64.7)
500,000-1,000,000	1	1	500,000-1,000,000	1
HIV Status			**HIV Status**	
HIV Positive	1.14(0.26-5.13)	0.9	HIV Positive	1.14(0.26-5.13)
HIV Negative	1	1	HIV Negative	1
Marital status			**Marital status**	
Married	3.29(0.15-74.6)	0.45	Married	3.29(0.15-74.6)
Single	2.98(0.15-74.6)	0.45	Single	2.98(0.15-74.6)
Divorced	-	-	Divorced	-
Widow	1	1	Widow	1

4.4.1 Survival of patients with skin cancer

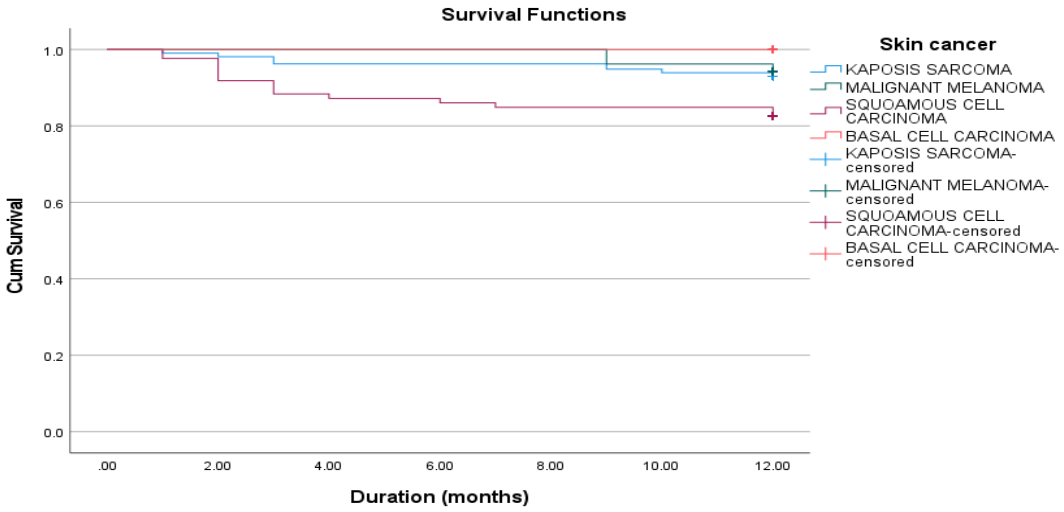
As can be deduced from Figure 3 below, the overall one–year survival rate of patients with skin cancer at the ORCI was 90.7%

Figure 3a. Survival of all patients with skin cancer



Survival of patients on Specific skin cancer type was assessed, the one-year survival rate of patients with the specific Skin cancer types were 93.4% for Kaposi Sarcoma, 94.3% for Malignant Melanoma, 82.6% for Squamous Cell Carcinoma and 100% for Basal Cell Carcinoma.

Figure 3b. Survival of patients by the type of skin cancer



CHAPTER FIVE

5.0 DISCUSSION, STRENGTHS OF THE STUDY AND STUDY LIMITATION

Introduction

This hospital based retrospective cohort study described the pattern, clinical presentation, time interval from presentation to definitive diagnosis and definitive treatment, treatment outcomes and their associated factors among patients with skin malignancies who were treated at the Ocean Road Cancer Institute (ORCI) in Dar Es Salaam, Tanzania from 2019 to 2023.

Social Demographic Characteristics of study participants.

The social demographic characteristics of the study participants provide valuable insights into the population accessing outpatient and inpatient treatment and rehabilitation services. The mean age of 49.9 years found in this study suggests that middle-aged individuals are more affected with skin cancer, similar to findings of the study done in South Africa which reported a mean age of mid 50's (32)**.** However, in a study done in Manipur India it was revealed that an advanced age groups in which skin cancers occurred were mainly the sixth, seventh and later decades (9,33). The differences might be due to the fact that most patients with skin cancer in this study had KS, which is mostly associated with HIV. Also, there is the fact that SCC and BCC are commonly seen among albinos, and thus there is early presentation of cancers as revealed in this study.

This study revealed that there was a predominance of males among patients with skin cancer. The results are similar with those from a study done in Sub Saharan Africa which also showed that the majority (68%) of patients with skin cancer were male(33). The results of male predominance might be due to the higher proportions of male working outdoors compared to females(34). However, female patients were predominant (68.5%) for patients with Squamous Cell Carcinoma.

Our study showed that majority (43%) were peasants, which imply that individuals may have limited access to health care and also do engage in occupations with a higher risk for skin cancer. Additionally, there is high proportion of participants with only primary education (52.7%) which underscores potential barriers to health literacy and awareness on health seeking behavior. This is similar to what was reported on health seeking behaviors among patients with skin disorders in Kano, Nigeria which reported that there was a statistically significant difference on urban respondents with educational attainment above primary school level compared to rural respondents (33). Hence our study and the study done in Kano, Nigeria had similar socioeconomic profiles of participants.

Pattern and Prevalence of Skin Malignancies.

In this study, Kaposi's Sarcoma emerged as the most prevalent cancer, accounting for 57% of all skin cancers, followed by squamous cell carcinoma (22%), malignant melanoma (16%), and then basal cell carcinoma (3%). The prevalence of these cancers does vary from that reported by the cancer statistics and WHO, 2018 (1,2). However, the results align with the reported epidemiology of Kaposi's Sarcoma, particularly in regions with a high prevalence of HIV/AIDS like in Tanzania (35) when compared to the global prevalence (36). However, in a study done among patients with albinism in Northern Tanzania, Malignant Melanoma was the most prevalent 67.5% followed by Kaposi's sarcoma 10.4% (7). This difference in prevalence is attributed by the fact that the study in northern Tanzania enrolled only patients with Albinism.

Our study showed that the prevalence of HIV among patients with skin cancer was relatively high, at 22.9%. This contrasts with findings from a retrospective cross sectional study in South America which showed that the prevalence of HIV among patients with skin cancer was 2.8% (37). The higher prevalence in our study might be due to the higher prevalence of HIV in our set up, and hence the inclusion of patients with Kaposi's Sarcoma, which is an AIDS defining cancer.

Our study did not find any patient who presented with malignancy from chronic ulcers, although literature shows that chronic venous ulcers and chronic diabetic ulcers have up to 2 % propensity of transformation to malignancies (1,2).

Clinical Presentation of Skin Malignancies

The detailed characteristics of different skin malignancies provide crucial clinical insights. In this study, the predominance of Kaposi's sarcoma on the lower limbs, with irregular-shaped and hyper pigmented lesions, is consistent with its reported typical presentation, often associated with immunosuppression (14). Similarly, the distribution and clinical features of Squamous Cell Carcinoma and Malignant Melanoma highlight the importance of thorough clinical examination, Dermoscopy and early biopsy in diagnosing these malignancies. Understanding the characteristic features of each malignancy can aid health care providers in timely diagnosis and appropriate management. These findings therefore offer insights into the diverse clinical characteristics of the different skin malignancies.

Time interval from symptoms onset to definitive treatment initiation at ORCI

The finding from this study that there was a median delay of 6 months from onset of symptoms to obtaining care at the ORCI is significant. It probably reflects the prevalence and the pattern of cancers seen, whereby rapidly progressing skin cancers such as malignant melanoma with high metastases rate, were relatively rare (38). Our study showed a slightly lower median delay time compared to the study done on patients pathway to cancer treatment in Tanzania, which reported a median time of 1 year (31). The difference could be attributed to some improvement in cancer care in Tanzania.

The distance from primary health centers, financial constraints and lack of knowledge about the disease condition were the major reported factors for the delay. This implies that there is need to decentralize advanced cancer care system in the country, government health financing and health education.

Outcomes of Cancer Treatment

Our study showed that the overall mortality was 11.3%. Furthermore, the study showed that there was a higher mortality of 14.5% among HIV positive patients compared to that of 10.2% among HIV negative patients. The higher mortality among HIV positive may be contributed by presence of opportunistic infection and treatment failure (39)

The predominance of radiotherapy among cured patients suggests its efficacy in treating certain types of skin malignancies, particularly Kaposi's Sarcoma,62.9% and Squamous Cell Carcinoma, 68.8%. However, the higher proportion of patients defaulting follow-up or deceased among those receiving chemotherapy underscores the need for comprehensive supportive care and close monitoring to improve treatment adherence and outcomes. However, an equal proportion of patients with Squamous Cell Carcinoma who died received chemotherapy and radiotherapy, compared to those with Malignant Melanoma, where a higher proportion of patients who died received chemotherapy (55.6%) compared to radiotherapy (44.4%). this implies that early treatment with radiotherapy have superior outcome compared to chemotherapy treatment in patients with Malignant Melanoma.

The varying treatment duration highlight the complexity of managing skin malignancies and the importance of individualized treatment plans based on disease stage and patient factors. This further highlights the importance of enhancing treatment availability at affordable costs and in various parts of the country in which most upcountry patients reside.

Factors associated with treatment outcomes

Our study showed that patients with no formal education have a reduced risk of being cured and an increased risk of dying from skin cancer in univariate analysis. However, the results were not significant when adjusted to confounders. This implies that formal education was not a strong predictor of mortality among patients with skin malignancies. Despite education level having not shown to be an independent predictor of outcome, we

have to underscore the role of educational level in improving cancer care and outcome, because literature has shown that education improves treatment outcomes in cancer patients (40).

The finding that the one-year survival of patients with skin cancer was good (being 100% for BCC, 93.4% for KS, 94.3% for MM, and 82.3% for BCC) implies that the available treatment modalities at the ORCI offer significant improvements in mortality. Indeed, the finding aligns well with those from other studies reported by WHO and global cancer statistics (1,2). It thus underscores the need for wider and easier access to treatment at the ORCI by patients with skin cancer.

Strengths of the study

This study was robust and it used a specific means to achieve the required inclusive sample size with much information at the shortest possible time to answer all research questions. The information obtained was analyzable and yielded significant information**.** This knowledge is important as it is the most recent filling the knowledge gap and have answers and recommendations in mediating several factors for cancer care in Tanzania. During interview of patients and relatives over the phone there was some recall bias from participants, since some were treated a long time ago so they had forgotten some important information. To mitigate this, participants who missed important information were excluded from the study.

Limitations of the study.

This study was conducted in a single center, which may restrict its generalization of the study findings and therefore, future research should aim for more comprehensive studies with larger sample sizes and longer follow up in various treatment centers in the country.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

In conclusion, our study has shown that in the past 5 years skin cancer was common in middle aged, males and peasants. The most common skin cancer was Kaposi's Sarcoma presenting in both upper and lower limbs. The second commonest type of cancer was squamous cell carcinoma which presented more on the scalp. Most of the patients were treated with radiotherapy which also resulted into good treatment outcome. Furthermore, the one-year survival was good, and varied by skin cancer type, and educational level appeared to impact treatment outcomes.

The prevalence of HIV among patients with skin cancer was high, with a subsequent higher mortality among these patients.

Unfortunately, most patients still report late for definitive treatment, with the commonly reported reasons being distance from a health facility, financial constraints and lack of awareness on the disease condition.

6.2 Recommendations

This study provides valuable epidemiological and clinical insights into the burden, characteristics, and outcomes of skin malignancies care among patients accessing health care services at the ORCI in Tanzania. On that basis, we recommend the following:

1. Provision of formal education be emphasized so as to improve awareness and treatment outcomes
2. Health care workers in the country need to be appraised of the clinical presentation of the various skin cancers so as to allow for early diagnosis and prompt referral of patients
3. Further multi-centred, prospective studies are needed to assess causes of delay as well as longer-term survival among patients with skin cancer.

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APPENDICES

APPENDIX I:DATA EXTRACTION TOOL.

1. SOCIODEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS

1. Study number: _____
2. Date of enrolment: _____
3. Sex: A) Male B) Female
4. Age of participant: _____
5. Admission status A) Inpatient B) Outpatient
6. Address: _____
7. Mobile number: _____ Next of kin Mobile number_____
8. Marital status: A. Single B. Married C. Divorced D. Cohabiting E. Widow F. Widower
9. Level of education A) No education B) Primary incomplete C) Primary complete

D) Secondary E) College/ University

10. Occupation: A). Unemployed B. Formal employment C). Self- employed (business owner) D). Casual laborel E) Peasant 6F) Works in mines/industries

11. Distance from residency to health facility A) < 5km B)5-20km C)>10km

12. Monthly income a) <50,000 b) 50,000-100,000 c) 100,000-500,000 d)500,000-1,000,000 e)>1,000,000

13.Oculocutaneous albinism A) YES B) NO

14. HIV STATUS A) Positive B) Negative

15. If positive last CD4 count……..

16. If HIV Positive last viral load,,,,,,,

17. HIV STAGE……..

2. **Other comorbid condition**

A) Hypertension B) myocardial infarction C) congenital heart disease

D) Stroke E) end stage renal disease F) Psychiatric condition G) BPH

H) Leukemia/ lymphoma I) Diabetes J) Illicit drug use K) Alcohol dependency

L)Neuromuscular/ paralysis M) Previous burn injuries on the malignant sites

N) Chronic diabetic foot ulcers O) Other medical conditions list ……..

3. Investigations at arrival.

A) Hemoglobin B) Platelet counts C) Neutrophil count

D) Creatinine…… E) Urea……F) Chest x ray findings…….

G) Abdominal ultrasound findings……

H) Histology results……

4**. First appearance of suspicious or nonhealing skin lesion?**

A) 1 month B) 2-5 Months C) 5-10 Months D) 10-12 months E) More than 12 months

5. Average time of illness before arrival at ORCI

A) 6months B) 6-12months C) 12-24months D) More than 24 months

6, When did you notice changes in present lesion prior to arrival at ORCI

a) 1 month ago b) 2months ago c) 3months D) 6 months E) 12 Months

7.**What was the cause associated with the lesion**

a) injury b) burn c) unknown d) others …..

8. Other changes in the lesion A) increase in size B) Very painful C) Discharge from lesion E) Others…….

9.Did you attend primary medical facility a) yes b) no

If no a) herbalist b) pharmacy c) private nurse/doctor d) self-medication e) disease not of hospital

10.Reasons for not attending health facility a) financial instability b) Belief c) it was not serious concern d) Others…….

11.Medications started in primary health care was

a) sufficient b) insufficient c) not helpful d) very costive e) others……

12.Time from diagnosis to attendance to ORCI in months……..

13 Reason for delay in attendance to ORCI

A) Treated by traditional healers B) Financial problem C) Self medications at home

D) No reason documented

14. Description of skin lesions

1. Cutaneous Primary lesion description A) Shape….. B) Colour….. C) Surface area…

2.Secondary lesion Description A) Shape….. B) Colour….. C) Surface area…….

15. Lesion manifestation

1. Site a) Scalp b) neck c) face d) ear e) nose f) eye lid g) upper limb h) trunk i) genitalia j) lower limbs k) unspecified site
2. Lesion occurrence A) Primary lesion B) Secondary lesion C) Recurrent Lesion
3. Size of lesion A) 0-1CM B)1-3CM C)3-5CM D) 5-10CM E) 10CM AND ABOVE
4. Number of lesions a)0-5 B) 5-10 C) More than 10
5. Extent Of invasion A) Only Skin involvement B) Systemic involvement
6. Percentage skin coverage A) 5-25% B) 25%-50% C)> 50%
7. Clinical Description of lesions…...
8. Multiple lesions with different description Explain……

16. Histological Diagnosis numbers each lesion

A) Malignant Melanoma B) Squamous cell carcinoma C) Basal cell carcinoma

D) Kaposis sarcoma E) Sebaceous Carcinoma

F) Melanocytic naevi G) neurofibroma H) dermatofibrosarcoma protuberance

I) Solar keratosis J) Secondary Lymphoma

16. Skin cancer staging at time of diagnosis Stage

a) T0 b) Tis c) T1b d) T2 e) T3 f) T4

16. Protective measures which were taken by patient

A) Use of sunscreen lotion and other sun protective methods A) YES B) NO

B) Use of long clothing A) YES B) NO

C) Use of UV light protecting lotion a) YES b) NO

Reasons if no sun screen protection use A) Lack of knowledge

A) Unavailability B) Lack of funds

C) Stigmatization eg wearing a hat all through the day

D) Others list…….

17. Treatment given at ORCI

A) Chemotherapy (systemic therapy) B) Radiotherapy C) Surgical excision

D) Both radiotherapy and chemotherapy E) Systemic treatment alone

E) Surgery plus radiotherapy F) surgery plus radiotherapy plus systemic therapy

18. Duration of treatment given number of weeks for each

A) Chemotherapy ……. B) Radiotherapy …….

19) Chemotherapy of choice given ……

20. Type of surgery done

A) Wide local excision B) Simple excision

C) With skin grafting D with flaps

E) Limb or extremity amputation F) Lymph node dissection

G) Skin Biopsy only

21. SURGERY SUCCESS RATE

A) Adequate tumor excision B) Inadequate excision C) Tumor free margin

22. Complications of surgery done

A) Surgical site infection B) Local recurrence

C) Loss of flaps D) Loss of skin grafting if done

E) Not documented

23. Factors for choice of treatment

A. Number of lesions B. Extent of invasion

C). Percentage skin coverage D). Systemic illness (Metastases)

24. Outcome of treatment given

1. Cured
2. Worsened/metastases
3. Relapse of same cancer
4. Died during treatment
5. Defaulted from follow up
6. Reason for defaulting a) cost of treatment b) Opting for other traditional treatment C) Worsening clinical condition

7.Time to death from last treatment in months……

8. Date of death……..

9. Date of discharge from Clinic …….

10. Date of last clinic attendance…….

25. Recurrence rate

A) Local recurrence B) Metastases recurrence

C) New site recurrence D) Stump site recurrence

25. If treatment discontinued reason for discontinuation

A) Worsening clinical status B) Anemia C) Adverse reaction from treatments

C) Others list

26. Factors associated with outcome

a) Poor adherence b) Adverse effects of treatment

c) Complications other than treatment associated list……

d) Defaulting or drop out during treatment e) Lack of Funding of treatment f) No reason documented

g) Living up country and could not afford follow up treatment

27. **Investigations at follow up clinic/ discharge for in patients**

A) Hemoglobin B) Platelet counts C) Neutrophil count

D) Creatinine E) urea F) potassium G) sodium

H) Chest x ray results ……...

I) Abdominal ultrasound results ……

H) Histology results after surgery …….

APPENDIX II: ETHICAL CLEARANCE FORM FROM MUHAS IRB OFFICE

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/1974 Date: 28/11/2023

MUHAS-REC-11-2023-1974
EMMANUEL JOHN EZEKIEL
COLLEGE OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: PATTERN, PRESENTATION AND TREATMENT OUTCOMES OF PATIENTS WITH SKIN MALIGNANCIES AT THE OCEAN ROAD CANCER INSTITUTE, DAR ES SALAAM, TANZANIA.

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 28/11/2023
EXPIRATION DATE OF APPROVAL: 28/11/2024

STUDY DESCRIPTION:
Purpose:

The purpose of this hospital based cross-sectional study with ambivalent approach retrospective as well as a prospective aspect is to describe patterns of skin malignancies clinical presentation treatment outcomes and their determining factors among patients attending the Ocean Road Cancer Institute in Dar Es Salaam Tanzania

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided:
https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014801.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Nahya Salim Mabsoud

Chairperson, MUHAS Research and Ethics Committee

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research, Publications & Innovations
Box 65001

APPENDIX III: INTRODUCTION LETTER OF TO ORCI HOSPITAL

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.116/2020 05th December, 2023

The Executive Director,
Ocean Road Cancer Institute,
P.O. Box 3592,
DAR ES SALAAM

Re: INTRODUCTION LETTER

We would like to inform you that the bearer of this letter is Emmanuel John Ezekiel with Reg. No. HD/MUH/T.116/2020 is a student at Muhimbili University of Health and Allied Sciences (MUHAS) "pursuing MMed. Internal Medicine.

As part of his studies, he will be doing an elective research titled: **"Pattern, Presentation and Treatment Outcomes of Patients with Skin Malignancies at the Ocean Road Cancer Institute Dar es Salaam, Tanzania."** He is being supervised by Prof. Mohammed Bakari from MUHAS and Dr. Emmanuel Nungu from ORCI.

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

We thank you for your cooperation.

Mr. Sebe Mohamed
For: DIRECTOR, POSTGRADUATE STUDIES

c.c Emmanuel John Ezekiel

APPENDIX IV: DATA COLLECTION CLEARANCE

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

OCEAN ROAD CANCER INSTITUTE

ORCI OCEAN ROAD CANCER INSTITUTE

On Reply Please Quote:

Ref: 10/VOL.XXI/189B

Date: 20th December, 2023

INSTITUTIONAL ACADEMICS, RESEARCH, PUBLICATIONS AND ETHICS COMMITTEE

Emmanuel John Ezekiel
Reg no: HD/MUH/T.116/2020
Mmed Internal Medicine
MUHAS

Re: Approval to conduct project "Pattern, Presentation and Treatment outcomes of patients with skin malignancies at Ocean Road Cancer Institute, DSM, Tanzania"

Reference is made to the above heading, this is to let you know that the Institute Academics, Research, Publications and Ethics Committee has granted you permission to conduct this study. This permission is for a period of one year.

Ethical considerations for the local implementation of the project has been carefully taken care of. Upon successful completion of the study, you are obliged to submit a copy of the final document of this research project to the IARPEC.

Yours Sincerely,

OCEAN ROAD CANCER INSTITUTE ACADEMIC UNIT P.O. Box 3592 DAR ES SALAAM

Dr Mamsau Ngoma
Academic Unit, ORCI